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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/344,226 06/25/99 CHIARELLO

R 2574.008US0

020227 HM12/0824
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EXAMINER

SOLOLA, T	
ART UNIT	PAPER NUMBER

1626
DATE MAILED: 08/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/344,226

Applicant(s)

Chiarello et al.

Examiner

Taofiq A. Solola

Group Art Unit
1626



☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-20 _____ is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-20 _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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Claims 1-20 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are written in functional language and therefore, broader than the enabling disclosure. For example, claim 1, recites "conjugating the fluorophore with an organic compound" (line 9, page 30), and claim 2, recites "reacting the organic compound and the fluorophore under covalent bond forming conditions" (lines 2-3). Therefore, claims 1-9, are indefinite. Claims 1-2, must recite specific steps as to how one of ordinary skill in the art would perform the conjugation and covalent bonding. The claims must recite the reagents, the reaction times and conditions involve in the processes. A claim must stand alone to define the inventions, and incorporation into the claims by express reference to the specification or an external source is not permitted. Ex parte Fressola, 27 USPQ 2d 1608, BdPatApp & Inter. 1993.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim

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does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1, lines 6-7 recites the broad recitation "Ra and Ra' are non-hydrogen substituents", the claim also recites on line 8, "Ra' includes a group reactive to derivatization", which is the narrower statement of the range/limitation. Therefore, claims 1-9, are indefinite. By deleting the narrower range/limitation the rejection would be overcome.

The phraseologies "Z includes the conjugated substance", line 18, claim 10; and "conjugated substance includes a phosphate ester", line 2, claim 12, are confusing, and therefore claims 10-20 are indefinite. By replacing the phraseology in claim 10, with "Z represents a linker plus the conjugated substance", and replace "includes" with "has" in claim 12, the rejection would be overcome.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al., US 4,647,675, in view of Arnost et al., US 4,900,686, and Kang US 5,846,737.

Applicants claim a process of conjugating rhodamine dyes of generic formula 1, having several substituents. For example, R1 to R14 are each H, alkyl or cycloalkyl; Ra is alkyl, cycloalkyl or aryl and Z "includes the conjugated substance". Also, R11 to R14 are each halogens. Mayer et al., teach rhodamine dyes having formula 1, with several substituents. For example, R, R1 to R5 are each alkyl, cycloalkyl; X and Y are each chlorine or bromine. See the abstract, specific species in columns 1-7, and claims 1-5. The difference between the instant invention and that of Mayer et al., is that applicants are claiming a process of making the conjugates while Mayer et al., do not teach a process of making the conjugates. However, Arnost et al., teach the process of making conjugates of rhodamines dyes having generic formula I (see examples 1-VII). Arnost et al., also teach several linking groups such as esters, aldehydes, cyanates, sulfide, etc. See the table in column 3. Kang teaches the process of conjugating rhodamine dyes, having formulae shown in columns 1-4, to bacteria, nucleic acid, etc. (see examples 1-17). Kang also, teaches that the conjugation could be performed with virus, yeast,

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and to immobilized solid or semi-solid support, such as polymer, membrane, polymeric particle, (microsphere), etc. See column 10, lines 10-18. The rhodamine dyes of Mayer et al., Arnost et al., and Kang are analogous compounds. The instantly claimed process would have been obvious from the teachings of Mayer et al., Arnost et al., and Kang because, the use of analogous reactants in a well known process is prima facie obvious. In re Durden, 226 USPQ 359, 1985. The motivation is to make additional fluorescent conjugates.

Claims 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al., US 4,647,675, in view of Arnost et al., US 4,900,686, and Kang US 5,846,737.

Applicants claim conjugated rhodamine dyes of generic formula 1, having several substituents. For example, R1 to R14 are each H, alkyl or cycloalkyl; Ra is alkyl, cycloalkyl or aryl and Z "includes the conjugated substance". Also, R11 to R14 are each halogens. Mayer et al., teach rhodamine dyes having formula 1, with several substituents. For example, R, R1 to R5 are each alkyl, cycloalkyl; X and Y are each chlorine or bromine. See the abstract, specific species in columns 1-7, and claims 1-5. The difference between the instant invention and that of Mayer et al., is that in the instant invention the compounds are being claim as conjugate while Mayer et al., do not teach the conjugates. However, Arnost et al., teach rhodamine dyes having generic formula I. Arnost et al., also teach that, the dyes are commonly used as conjugates in biological diagnostic assays, and that the most commonly use dyes are fluorescent dyes (column 1, lines 1-40). Kang teaches rhodamine dyes having formulae shown in columns 1-4, and their method of use as conjugate of peptides, proteins nucleotides, etc. (column 1, lines 1-4). Kang

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also, teaches the conjugation of rhodamine dyes to bacteria, virus, yeast, and to immobilized solid or semi-solid support, such as polymer, membrane, polymeric particle, (microsphere), etc. See column 10, lines 10-18. Therefore, the instant invention is prima facie obvious from the teachings of Mayer et al., Arnost et al., and Kang. One of ordinary skill in the art would have known to conjugate the rhodamine dyes of Mayer et al., at the time the instant invention was made. The motivation is to make additional fluorescent conjugates.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola whose telephone number is (703) 308-4690.

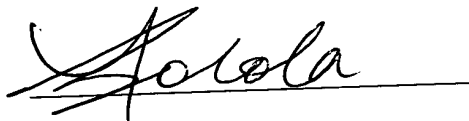
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

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A handwritten signature in black ink, appearing to read "Solola", is written over a horizontal line.

Taofiq A. Solola

Patent Examiner

Group 1626

August 18, 2000